PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

François CHRETIEN
RHONE-POULENC AGROCHIMIE
Industrial Property Dept.
P.O. Box 9163
F-69263 Lyon Cedex 09
FRANCE

PCT

[rubber stamp]

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 61.1)

Date of mailing (*day/month/year*)	30.10.97
Applicant's or agent's file reference PH 95039	IMPORTANT NOTIFICATION

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/FR 96/01125	18/07/1996	19/07/1995

Applicant
RHONE-POULENC AGROCHIMIE et al

1. This applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the International preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. (+ 49-89) 2399-0, Tx: 523656 epmu d Fax: (+ 49-89) 2399-4465	C. Vullo (signature) Telephone No. 8052

Translation

9

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PH 95039	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/FR96/01125	International filing date (*day/month/year*) 18 July 1996 (18.07.1996)	Priority date (*day/month/year*) 19 July 1995 (19.07.1995)
International Patent Classification (IPC) or national classification and IPC C12N 15/54, 15/82, A01H 5/00		
Applicant RHONE-POULENC AGROCHIMIE		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
07 February 1997 (07.02.1997)	30 October 1997 (30.10.1997)
Name and mailing address of the IPEA/EP European Patent Office D-80298 Munich, Germany Facsimile No. 49-89-2399-4465	Authorized officer Telephone No. 49-89-2399-0

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR96/01125

I. Basis of the report

1. This report has been drawn on the basis of (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

☒ the international application as originally filed.

☐ the description, pages _____, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☐ the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. _____, filed with the letter of _____,
Nos. _____, filed with the letter of _____.

☐ the drawings, sheets/fig _____, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	4-6, 11 and 15-18	YES
	Claims	1-3, 7-10 and 12-14	NO
Inventive step (IS)	Claims		YES
	Claims	1-18	NO
Industrial applicability (IA)	Claims	1-18	YES
	Claims		NO

2. Citations and explanations

1) Reference is made to the following documents:

D1: Annual Meeting of the American Society of Plant Physiologists, July 28-August 1, 1991, Plant Physiol. Bethesda, vol. 96 (1 suppl.), abstract 592.

D2: WO-A-95/06128

D3: WO-A-91/04323

D4: WO-A-92/06201

D5: EP-A-0 293 358

2) The subject matter of claims 1-3, 7-10 and 12-14 does not satisfy the criterion of PCT Article 33(2).

D1 describes an EPSPS protein of plant origin containing a Threonine substitution in position 102 by Isoleucine ("T102I"). D1 therefore deprives the subject matter of claim 9 of novelty.

D2 describes a gene originating from Zea mays and coding for an EPSPS enzyme containing a Threonine substitution in position 102 by an Isoleucine and a substitution of Proline in position 106 by a Serine (cf.

page 119, second paragraph). D2 also describes the production of vectors containing this muted gene under the control of a promoter of plant origin (page 119, line 16 to page 120, line 20). These vectors are used to transform plant cells (cf. page 150, last paragraph; Example 26).

D2 therefore deprives the subject matter of claims 1-3, 7-10 and 12-14 of novelty.

3) The subject matter of claims 4-6, 11 and 15-18 does not satisfy the criterion of PCT Article 33(3) for the following reasons.

Before the priority date of the application, it was known that the substitution of EPSPS Glycine 101 by Alanine offers resistance to glyphosate (cf. D3, page 4, last paragraph; D4, page 4, second paragraph; and D5, page 4, lines 4-13). The addition of this substitution, the effect of which is known, to the muted enzyme described in D1 and D2 with a view to preserving or increasing resistance to glyphosate cannot therefore be considered to be based on an inventive step.

The EPSPS gene originating from Salmonella typhimurium was known before the priority date of the present application (cf. D3, Figure 1; D4, Figure 1; D5, Figure 2). Since no particular advantage appears to be conferred on it by its origin, this gene only appears to represent an alternative equivalent to the gene of plant origin described in D2.

The same is true of the choice of a plant virus promoter, the use of which in vectors comprising a muted

EPSPS gene is widespread (cf. CaMv 35S promoter in D3-D5), instead of the plant promoter used in D2.

Since the regeneration of plants based on transformed plant cells is a purely conventional practice, the subject matter of claims 15 and 16 is also devoid of inventive step in view of D2.

The use of a herbicide with EPSPS as a target for a plant regenerated in this way, which therefore carries a muted EPSPS gene, in order to test resistance to the herbicide in question is also obvious for a person skilled in the art.

For these reasons, claims 4-6, 11 and 15-18 are devoid of inventive step.

4) The subject matter of claims 1 to 18 is industrially applicable as defined in PCT Article 33(4).

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Contrary to the requirements of PCT Rule 5.1(a)(ii), the description does not indicate the relevant prior art disclosed in documents D1-D5 and does not cite these documents.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PH 95039	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/FR 96/ 01125	International filing date (day/month/year) 18/07/1996	Priority date (day/month/year) 19/07/1995
International Patent Classification (IPC) or national classification and IPC C12N15/54		
Applicant RHONE-POULENC AGROCHIMIE et al		

1. This internal preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets including this title page.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings amended during international preliminary examination and/or containing rectifications made before this Authority (see Rule 70.16 and Instruction 607 of PCT Administrative Instructions).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement according to Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
07/02/1997	30.10.97
Name and mailing address of the IPEA/ European Patent Office D-80298 Munich Tel. (+ 49-89) 2399-0, Tx: 523656 epmu d Fax: (+ 49-89) 2399-4465	Authorized officer (illegible signature) Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR96/01125

I. Basis of the report

1. This report has been drawn up on the basis of the following elements (The replacement sheets received by the receiving office in response to an invitation according to Article 14 are considered in the present report as "originally filed" and are not annexed to the report as they contain no amendments)

☒ the international application as originally filed.

☐ the description, pages _____ , as originally filed,
pages _____ , filed with the demand,
pages _____ , filed with the letter of _____ .
pages _____ , filed with the letter of _____ .

☐ the claims, No. _____ , as originally filed,
No. _____ , as amended under Article 19,
No. _____ , filed with the demand,
No. _____ , filed with the letter of _____ .
No. _____ , filed with the letter of _____ .

☐ the drawings, sheets/fig _____ , as originally filed,
sheets/fig _____ , filed with the demand,
sheets/fig _____ , filed with the letter of _____ .
sheets/fig _____ , filed with the letter of _____ .

2. The amendments have resulted in the cancellation of:

☐ the description, pages: _____
☐ the claims No.: _____
☐ the sheets of drawings/figures No.: _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2.c)

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR96/01125

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty	Claims	4-6, 11, 15-18	YES
	Claims	1-3, 7-10, 12-14	NO
Inventive Step	Claims		YES
	Claims	1-18	NO
Industrial Applicability	Claims	1-18	YES
	Claims		NO

2. CITATIONS AND EXPLANATIONS

1) Reference is made to the following documents:

D1 : Annual Meeting of the American Society of Plant Physiologists, July 28- August 1, 1991, Plant Physiol. Bethesda, vol. 96 (1 suppl.), abstract 592.
D2 : WO-A-95/0618
D3 : WO-A-91/04323
D4 : WO-A-92/06201
D5 : EP-A-0 293 358

2) The subject of claims 1-3, 7-10 and 12-14 does not satisfy the criterion set out by Article 33(2) PCT.

D1 describes an EPSPS protein of plant origin comprising a substitution of Threonine at position 102 by Isoleucine ("T102I"). D1 therefore deprives the subject of claim 9 of novelty.

D2 describes a gene derived from Zea mays and encoding an EPSPS enzyme comprising a substitution of Threonine at position 102 by an Isoleucine and a substitution of Proline at position 106 by a Serine (cf. page 119, second

paragraph). D2 also describes the production of vectors comprising this mutated gene under the control of a promoter of plant origin (page 119, line 16- page 120, line 20). These vectors are used for the transformation of plant cells (cf. page 150, last paragraph; Example 26).

D2 therefore deprives the subject of claims 1-3, 7-10 and 12-14 of novelty.

3) The subject of claims 4-6, 11 and 15-18 does not satisfy the criterion set out by Article 33(3) PCT for the following reasons.

It was known, before the priority date of the application, that the substitution of Glycine 101 of EPSPS by Alanine confers resistance to glyphosate (cf. D3, page 4, last paragraph; D4, page 4, second paragraph and D5, page 4, lines 4-13). The addition of this substitution, whose effect is known, to the mutated enzyme described in D1 and D2 so as to conserve or increase the resistance to glyphosate cannot therefore be considered to result from an inventive approach.

The EPSPS gene derived from Salmonella typhimurium was known before the priority date of the present application (cf. D3, Figure 1; D4, Figure 1; D5, Figure 2). Since no particular advantage appears to be conferred on it by virtue of its origin, this gene appears to represent only an alternative equivalent to the gene of plant origin described in D2.

The same applies to the choice of a plant virus promoter, whose use in vectors comprising a mutated EPSPS gene is very widespread (cf. CaMV 35S promoter in D3-D5), in place of the plant promoter used in D2.

The regeneration of plants from transformed plant cells being a purely conventional practice, the subject of claims 15 and 16 also lacks an inventive step in the light of D2.

The application of a herbicide having EPSPS as target to a plant thus regenerated, which therefore carries the mutated EPSPS gene, so as to test the resistance to the herbicide in question, is also obvious for persons skilled in the art.

For these reasons, claims 4-6, 11 and 15-18 lack an inventive step.

4) The subject of claims 1 to 18 is susceptible of industrial application as defined by Article 33(4) PCT.

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Contrary to what is required by Rule 5.1 a) ii) PCT, the description does not indicate the relevant prior state of the art disclosed in documents D1-D5 and does not cite these documents.

Rhône-Poulenc Agrochimie

Descriptive abstract

Glyphosate resistance gene

1. Mutated glyphosate resistance gene.

2. EPSPS gene comprising at least one substitution of threonine 102 by isoleucine.

3. It can be used for producing glyphosate-resistant transformed plants.